

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/06769

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5,9
	No:	Claims	1-4,6-8,10
Inventive step (IS)	Yes:	Claims	5,9
	No:	Claims	1-4,6-8,10
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

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2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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Re Item IV

Lack of unity of invention

This International Examining Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 4,5,9(all complete),1-3,7,8(all partially)

Compounds according to formula I, wherein at least one of R8 and R9 is -CH₂-sec-amine, their preparation and pharmaceutical compositions.

2. Claims: 6,10(complete)1-3,7,8(all partially)

Compounds according to formula I, wherein R8 and R9 are both H, their preparation and pharmaceutical compositions.

Reasoning

- 1)Reading the claims in the light of the description the problem to be solved could initially be considered to be the provision of compounds having antifungal activity.
- 2)This problem has been solved by a plurality of solutions as defined in claim 1, relating to cyclohexapeptides of the echinocandin type. The application further relates to pharmaceutical compositions containing said compounds, their preparation and use.
- 3)This plurality of solutions might, a priori, be considered as satisfying the requirements of unity in which the antifungal activity provides the special technical feature linking these different solutions.
- 4)However at the first priority date of the application compounds having antifungal activity were already well-known in the prior art, as can be exemplified by the documents cited in the ISR and which can be illustrated by WO9527074 (D1).
- 5)In the light of these documents, it is considered that a common technical link based on the antifungal activity exhibited by the compounds of the application which could be the unifying concept is no longer present.
- 6)The objective problem in view of D1 could therefore be considered to be the provision of alternative compounds having antifungal activity.

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7) Therefore further unified solutions should relate to groups of compounds sharing a common structural element which may be regarded as the special technical feature providing unity; this special technical feature should be an essential structural part common to all of the embodiments of the claimed invention (and responsible for the inventive effect) and which is absent from any solution to the same problem disclosed in the prior art.

8) Regarding all of the proposed solutions as a whole, as defined in independent claim 1, the only common invariant structural features which can be detected are the structure of general formula I, disregarding the variable substituents R1-R9 and R'.

9) It is considered that D1 discloses compounds which possess the same structural features as those described above and are intended for the solution of the same problem as that underlying the present application. For these reasons it is considered that the compounds claimed in the present application lack any common structural feature which could be regarded as the special technical feature providing unity to the application.

10) As no other technical features can be distinguished which, in the light of the prior art, could be considered as special technical features on which a unifying concept could be based, there is lack of unity between the plurality of claimed inventions defined in the compound claims of the present application (see Rule 13.1 PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO-A-9527074

D2: J. Antibiot., Vol. XL, No. 3, 275-280

D3: WO-A-9622784

D4: WO-A-9421677

D5: US-A-5914313

Cited as in 409

include in US →

1 cited US version of these 2

Other 3 refs don't expressly teach claim 10 comp.

→ Cited as in 409

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1) subj. 1

I. NOVELTY

D1 discloses cyclohexapeptides of the present type which are characterized, inter alia, by the presence of at least one disubstituted aminoalkyl group as substituent in the tyrosine ring (see especially claim 1, substituent R8). The examiner is guided by the principle according to which the disclosure in a prior document likely to affect the novelty of a claim is not necessarily limited to the specific working examples, but also comprises any reproducible technical teaching described in the document. In order to acknowledge novelty to the not specifically disclosed overlapping subject-matter it is considered to be necessary that said subject-matter is based on a new technical teaching. It is at present not apparent whether the subject-matter of the overlapping area relates to a new technical teaching (based on a new "technical element") with respect to the prior art and therefore novelty cannot be recognised for said overlapping area. Consequently the claims 1-4, 7 and 8 are considered to lack novelty under Art. 33(2) PCT.

5 9+10

II. INVENTIVE STEP

1) The closest prior art is considered to be D1 disclosing, as discussed in the previous section, cyclohexapeptides of the present type which are characterized, inter alia, by the presence of at least one disubstituted aminoalkyl group as substituent in the tyrosine ring (see especially claim 1, substituent R8).

2) The novel subject-matter of the present application essentially differs from said prior art in the presence of a cyclic secondary aminomethyl group as substituent of the tyrosine ring. Said compounds exhibit antifungal activity and have a good water solubility.

3) The problem to be solved may therefore be considered to be the provision of alternative antifungal compounds having a cyclopeptide structure and a good solubility in water.

4) It is considered that in the prior art the present cyclic secondary aminoalkyl group as substituent of the tyrosine ring neither has been indicated nor suggested.

5) Consequently an inventive step can be acknowledged under Art. 33(3) PCT for the subject-matter of claim 5 and also for their production process as defined in claim 9.

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2. subj.

I. NOVELTY

→ 1) D2 discloses the basic compound Mulundocandin, wherein the positions corresponding to R1 and R3 in the general formula I of the application are both hydroxy. Hence the claims 1-3 and 6-8 lack novelty under Art.33(2) PCT.

→ 2) D3 discloses cyclohexapeptides encompassed by the present formula I, which are characterized, inter alia, by a facultative substituted aminomethyl group or a nitril group in the corresponding position R1 and a sidechain R' which can comprise a C9-C21 alkyl group. Furthermore the process for preparing said compounds (e.g., see pages 11-12) includes the steps a-c of claim 10.

The examiner is guided by the principle according to which the disclosure in a prior document likely to affect the novelty of a claim is not necessarily limited to the specific working examples, but also comprises any reproducible technical teaching described in the document. In order to acknowledge novelty to the not specifically disclosed overlapping subject-matter it is considered to be necessary that said subject-matter is based on a new technical teaching. It is at present not apparent whether the subject-matter of the overlapping area relates to a new technical teaching (based on a new "technical element") with respect to the prior art and therefore novelty cannot be recognised for said overlapping area. Consequently the claims 1-3, 6-8 and 10 are considered to lack novelty under Art.33(2) PCT.

→ 3) Document D4 relates to cyclohexapeptides of the present type, comprising in position R1 a substituted amino group. In view of this prior art the claims 1-3 and 6-8 are considered not to fulfil the requirements of Art.33(2) PCT.

→ 4) D5 also discloses cyclohexapeptides, which in this document are characterized by a substituted alkyloxy group in position R1. For reasons mentioned in the preceding part D5 renders the claims 1-3, 6-8 not novel under Art.33(2) PCT.

Re Item VII

Certain defects in the international application

In order to meet the requirements of Rule 5.1(a)(ii) PCT the documents D1-D5 should have been discussed in the description.

Re Item VIII

Certain observations on the international application

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1) An independent claim should clearly specify all of the essential features needed to define the invention (PCT Guidelines C-III, 4.1-4.7a). The present claims 1, 2, 4, 6, 9 and 10 contain expressions like "(substituted) aryl" and "(substituted) heterocycle", rendering the scope of said claims unclear under Art. 6 PCT. It is true that under circumstances such expressions can be acceptable in product claims, e.g. in definitions of non-essential features like protecting groups. However in the present case said expressions are also used to define structural features that are considered to be characteristic for the present compounds. Consequently the claims 1, 2, 4, 6, 9 and 10 are considered not to fulfil the requirements of Art. 6 PCT.

2) The claims should be supported by the description (PCT Guidelines CIII, 6.1-6.6). That is, the claims should be a fair generalization over the experimental data. However at present the examples comprise only a very small part of the compounds claimed, which part is moreover not evenly distributed over the whole claimed area, whereas even any experimental data relating to their activity is lacking. Consequently the claims 1-10 are considered to contravene Art. 6 PCT.